Metastatic thymoma: a case report and immunohistological analysis

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SUMMARY A patient with metastatic lymphocyte predominant thymoma was studied and an immunohistological analysis of frozen and paraffin sections was performed. The immunophenotype of the lymphoid cells was similar to that of primary thymomas and T cell lymphoblastic lymphomas. The epithelial cells reacted with an anticytokeratin monoclonal antibody. The results have diagnostic implications for the histopathologist using immunohistochemistry as a diagnostic aid and it is concluded that a panel of monoclonal antibodies against both lymphoid and epithelial markers should be used for immunohistological typing of tumours of uncertain histogenesis.

Thymomas are neoplasms of thymic epithelial cells with a variable associated lymphocytic component, 1 which is considered to be reactive or secondary to local influencing factors. Recent studies on the immunohistology of primary thymomas²⁻⁴ have confirmed the findings of earlier reports based on E rosetting⁵—that is, the associated lymphocytes are T cells. Such studies have also shown that these lymphoid cells have a phenotype similar to that of cortical thymocytes.

Thymomas rarely metastasise, 16 and as far as we are aware there have been no reported studies of the immunophenotype of the lymphoid cells in metastatic thymoma. We report here a case of metastatic thymoma that was analysed immunohistologically and discuss the importance of the results with respect to the known phenotype of primary thymomas and their importance to the histopathologist using immunohistochemistry as a diagnostic aid.

Case report

A 52 year old woman presented with enlarged cervical lymph nodes. Radiological examination showed a large mediastinal mass. A left cervical lymph node was resected, and part of it fixed in 4% neutral buffered formaldehyde and processed for paraffin sections; another part was snap frozen and sections cut for immunohistological studies.

Examination of the patient's medical history showed that she had been treated seven years previously with radiotherapy for a right sided medias-

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recent presentation.

Histological examination of paraffin sections of the cervical lymph node stained with haematoxylin and eosin showed a few residual lymphoid follicles, but most of the node was replaced with a diffuse infiltrate of cells. This infiltrate consisted of two populations: a predominance of small lymphocytes and a background population of larger cells with fine nuclear chromatin, usually a single eosinophilic nucleolus, and fairly abundant cytoplasm (Fig. 1). The differential diagnosis lay between metastatic lymphocyte predominant thymoma and T cell lymphoblastic lymphoma. A definitive diagnosis of metastatic lymphocyte predominant thymoma was made only when the results of immunohistochemical staining were

tinal mass that had presented with obstruction of the superior vena cava. A biopsy specimen of this mass at

the time had features of lymphocytic thymoma. There

was no other notable medical history; in particular,

there was no evidence of myasthenia gravis, red cell

aplasia, or hypogammaglobulinaemia. She had been

well during the interval from her operation to her

Immunohistochemical staining was performed by an indirect immunoperoxidase technique, as described fully elsewhere.7 The Table gives the reactivity of the epithelial and lymphoid components of the metastatic thymoma with a panel of monoclonal antibodies. The monoclonal antibodies used were obtained from the following sources: F10-89-4 and F8-11-13 from

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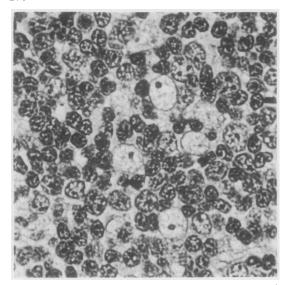


Fig. 1 Scattered large cells with fine nuclear chromatin and a single nucleolus are admixed with diffuse infiltrate of small lymphocytes. Haematoxylin and eosin stained paraffin section. × 675.

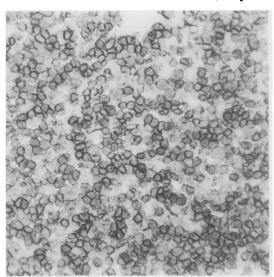


Fig. 2 Frozen section stained with OKT6 shows strong reactivity with majority of lymphocytes. × 320.

J Fabre, Blond McIndoe Centre, East Grinstead; OKT6, OKT11, OKT3, OKT4, OKT8, and OKM1 from Ortho Diagnostics; Leu4 and Leu10 from Becton Dickinson; DA6231 from K Guy, Medical Research Council Clinical and Population Cytogenetics Unit, Western General Hospital, Edinburgh; anticytokeratin from Lab Systems; and Dako-EMA, Dako-B, and Dako-LC from Dakopatts. Immu-

nohistochemical staining was carried out on frozen sections with each of these monoclonal antibodies. In addition, paraffin sections were stained with Dako-LC, F8-11-13, anticytokeratin, and Dako-epithelial membrane antigen, the results obtained being similar to those seen on frozen sections.

Most of the lymphoid cells reacted with the leucocyte common monoclonal antibody F10-89-4 and

Reactivity of the lymphoi	d and epithelial cell	of metastatic thymoma w	ith monoclonal antibodies
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Antibody	Specificity	Lymphocytes	Epithelial cells
F10-89-4	Leucocyte common antigen	+++	_
Dako-LC	Leucocyte common antigen	+++	-
F8-11-13	Leucocyte common antigen	+	_
OKT6	Cortical thymocytes	+++	_
OKTII	'E' receptor	+++	_
OKT3	Pan T cells	+ +	_
UCHT1	Pan T cells	+++	_
Leu4	Pan T cells	+++	-
OKT4	Helper T cells	+++	_
OKT8	Suppressor T cells	+++	_
DA6 231	MHC class II DP and DR	+	+++
Leu10	MHC class II DQ	+	+++
Dako-B*	Pan B cells	_	_
OKMI	Macrophages	_	-
Anti-cytokeratin	Cytokeratin	_	+++
Dako-EMA	"Épithelial membrane antigen"		_

MHC = Major histocompatibility complex.

^{-=&}lt;5%; +=5-30%; ++=30-60%; +++=>60% positively staining cells. *Dako-B stained a few residual lymphoid follicles.

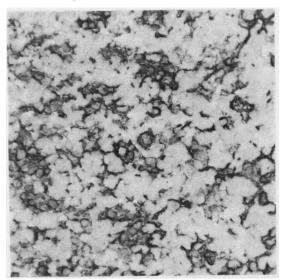


Fig. 3 Frozen section stained with DA6 231 (major histocompatibility complex Class II DP and DR) shows strong reactivity with large cells and dendritic processes. × 320.

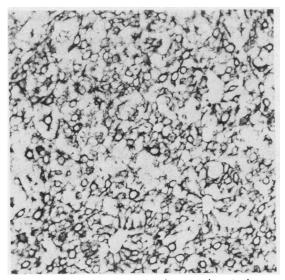


Fig. 4 Paraffin section stained with anticytokeratin shows large numbers of epithelial thymoma cells with dendritic processes. × 160.

Dako-leucocyte common, but only scattered lymphocytes reacted with F8-11-13, which recognises the high molecular weight form of the leucocyte common antigen not normally expressed by cortical thymocytes. BOKT6 and OKT11 reacted strongly with most lymphoid cells (Fig. 2). The pan T cell markers,

Leu4 and UCHT1, showed strong reactivity with most lymphoid cells in a similar way to that seen with OKT6, but OKT3 reacted only with about 60% of the lymphoid cells. OKT4 and OKT8 stained most lymphoid cells. Scattered collections of lymphocytes reacted with the major histocompatibility complex class II monoclonal antibodies, Leu10 and DA6 231. Most lymphoid cells were also shown to be positive for terminal deoxynucleotidyl transferase by immunofluorescence.

Epithelial cells did not react with any of the T or B lymphoid cell markers. Leu 10 and DA6 231 reacted strongly with the epithelial cells and also showed strong staining of a dendritic network (Fig. 3). This is consistent with the observation that thymomas contain S100 positive cells that appear to be interdigitating dendritic cells. Cytokeratin reacted strongly with the epithelial cells and dendritic processes arising from these cells (Fig. 4).

There was no reactivity with either the lymphoid or epithelial components of the thymoma with DakoB, OKM1, or Dako EMA.

Discussion

As far as we are aware this is the first reported case of metastatic thymoma using a detailed immuno-histological study. The lymphoid cells expressed a cortical thymic phenotype, most cells reacting with the monoclonal antibodies OKT6, OKT11, OKT4, and OKT8 but failing to react with F8-11-13. Most of the lymphoid cells were also shown to be positive for terminal deoxynucleotidyl transferase by immunofluorescence. This suggests that the neoplastic epithelial cells in metastatic thymoma are capable of producing a lymphopoietic environment similar to that of the normal thymus.

The immunophenotype of the lymphoid cells in this patient with metastatic thymoma and in primary thymomas is similar to that of T cell lymphoblastic lymphoma. 9-11 In most cases of thymoma the epithelial component of the neoplasm is readily identifiable, as are other histological features such as rosette formation.1 In cases of lymphocyte predominant thymoma, however, the epithelial component may be less easily recognised and perhaps misinterpreted as the reactive histiocytic cells often seen in lymphomas. The finding that the epithelial cells of metastatic thymoma stain strongly with an anticytokeratin monoclonal antibody agrees with other reports in which the epithelial cells of primary thymomas have been shown to react with antikeratin antibodies^{3 4 12} and an anticytokeratin monoclonal antibody, CAM5-2.13 This has obvious diagnostic implications for the histopathologist using immunoperoxidase techniques to help classify lymphomas. By the use of a standard

panel of monoclonal antibodies against lymphoid markers a lymphocyte predominant thymoma would show the phenotype of a T cell lymphoblastic lymphoma with a scattered background population of major histocompatibility complex class II positive large cells. If anticytokeratin antibodies are not used the true epithelial nature of these cells may be overlooked and the thymomatous nature of the lesion missed.

As previously suggested by ourselves and other authors, ¹⁴⁻¹⁸ to decrease the possibility of misinterpretation and erroneous diagnosis it is therefore imperative that for routine diagnosis a panel of monoclonal antibodies against both lymphoid and epithelial markers should be used for immunohistological typing of tumours of uncertain histogenesis.

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